Neurodevelopmental and Academic Outcomes in Children With Orofacial Clefts: A Systematic Review

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abstract

CONTEXT: Children with orofacial clefts (OFCs) are reported to have worse neurodevelopmental outcomes than unaffected peers, although study methodologies and findings are highly variable and trends in outcomes by age remain unexplored.

OBJECTIVE: To examine the strength of the evidence and explore trends in neurodevelopment by age.

DATA SOURCES: A systematic review was conducted of studies published from January 1, 1980, through November 3, 2017.

STUDY SELECTION: Studies were independently screened by the authors and included in the review if they met predetermined eligibility criteria: (1) children and/or youth (<25 years) with OFCs were studied, and (2) neurodevelopmental or academic outcomes were included.

DATA EXTRACTION: The authors independently evaluated study quality and extracted outcome data.

RESULTS: Thirty-one studies involving 10 143 patients with OFCs and 2 017 360 controls met eligibility criteria. Although the quality of the studies varied, patients with OFCs consistently performed worse than their peers on neurodevelopmental and academic measures. In infancy, differences were observed on multiple developmental outcomes (eg, cognition, motor skills, and language), and in later childhood and adolescence, differences were manifest on several indicators of academic achievement (eg, use of special education services, grades, and scores on standardized measures).

LIMITATIONS: Heterogeneity in study designs, methods, and outcomes prevented statistical pooling and modeling for meta-analysis.

CONCLUSIONS: Children with OFCs exhibit neurodevelopmental and academic deficits compared with their unaffected peers. Although the nature of these deficits changes with development, differences are observed from infancy through adolescence. Clinicians should monitor neurodevelopment in children with OFCs and support them appropriately.

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Dr Gallagher conceptualized and designed the study, designed the data collection instruments, reviewed the articles, extracted data, and drafted the initial manuscript; Dr Collett conceptualized and designed the study, reviewed the articles, and extracted data; and all authors reviewed and revised the manuscript, approved the final manuscript as submitted, and agree to be accountable for all aspects of the work.

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Orofacial clefts (OFCs) affect 1 in 700 live births, making them the most common craniofacial malformation and second only to structural heart defects among all birth defects. OFCs include cleft lip (CL), cleft lip and palate (CLP), and cleft palate (CP) only. Authors of numerous studies have reported that children with OFCs have worse neurodevelopmental and academic outcomes than unaffected peers. The underlying reasons for these deficits are unclear. Hypothesized mechanisms include functional consequences of oral clefting (e.g., feeding difficulty, eustachian tube dysfunction, or speech impairment), treatment factors (e.g., frequent school absences), repeated anesthesia exposures, and social stigma (e.g., differential treatment based on appearance or speech and/or voice quality). Researchers also suggest that patients with OFCs may have structural brain differences and differences in outcome depending on cleft laterality, implying that a cleft might be a marker for aberrant brain development. Although these findings are relatively consistent in showing that children with clefts perform worse than their peers, this literature has been variable in terms of quality, methodology, and outcomes studied. For example, study designs have ranged from small case series to population-based studies. Outcomes include clinician-administered validated assessments, existing data in the form of standardized educational test scores and graduation rates, and parent-reported outcomes. Study heterogeneity raises questions about the robustness of the findings and complicates efforts to translate findings into patient care. For example, implementing developmentally informed, evidence-based screening and intervention strategies requires better understanding of potential targets as a function of child age and clinical characteristics.

To our knowledge, this is the first systematic review of the literature on neurodevelopmental outcomes and oral clefting and the first to address neurodevelopmental trends by child age. An earlier systematic review was focused on the psychosocial effects of OFCs and concluded that most people with OFCs do not experience major psychosocial sequelae. Authors of narrative reviews have discussed sequelae of clefts, including the impact on academics and psychological adjustment, but these were not systematic reviews and were therefore subject to selection bias. Because of the variable quality and the range of outcomes studied, a systematic review that synthesizes and critically appraises previous findings would help providers understand the associated risk of lower academic outcomes for patients with OFCs, identify specific areas of vulnerability by age, and provide appropriate support for this patient population.

Our goals in this review were to analyze the quality of studies of neurodevelopmental and academic outcomes in children with OFCs, to understand outcomes as a function of developmental stage, and to explore potential targets of interventions to improve outcomes.

METHODS

Search Strategy and Selection

The search strategy was developed with a hospital librarian and investigators with specialized training in pediatrics (E.R.G.) and psychology (B.R.C.) to identify articles in which neurodevelopmental and academic outcomes in children with OFCs are reported. The review was registered on PROSPERO on December 5, 2017 (CRD42017079689). Search terms included “cleft palate,” “cleft lip,” or “orofacial cleft” combined with neurodevelopmental disorders, developmental disabilities, achievement, education, language development, school performance, or educational measurements. The search strategy was applied to the Medline, Embase, PsycINFO, and Cumulative Index to Nursing and Allied Health databases from January 1, 1980, to November 3, 2017 (the Cumulative Index to Nursing and Allied Health’s first citation retrieved was from 1991). The start date coincided with routine use of a revised surgical technique for palatoplasty in the 1970s. An earlier systematic review of the literature on neurodevelopmental or academic outcomes in patients aged <25 years with OFCs were reported that were published in English. These included studies of infant and/or toddler development, language, and cognition or academic achievement. We included studies with descriptive outcomes (e.g., graduation rate) as well as those using standardized, clinician-administered measures (e.g., the Wechsler Preschool and Primary Scale of Intelligence) and noted differences in our quality assessment. If multiple publications included the same cohort, we included studies with unique outcome measures. To control for patients’ access to care, we limited our review to studies in middle- to high-income economies. We included studies without a control group but accounted for this in the quality assessment. We excluded small case series (≤10 cases), qualitative studies, and studies comparing surgical approaches. We also excluded studies addressing speech intelligibility in contrast to expressive or receptive language. However, an article in which both phonologic outcome and a validated measurement of a developmental outcome were reported would be included only for developmental outcomes. We excluded reviews, dissertations, book chapters, and conference abstracts, although we attempted to find publications by these authors. Two authors

Data Extraction and Quality Assessment
Quality assessment criteria included patient selection (population versus clinic based, adequate demographic information for participants and data reported to discern participation rate); clinical criteria (method of identifying syndromic patients and inclusion of hearing data); study design (homogeneous group versus control group); and validity of the outcome. We included hearing data as a quality measure because conductive hearing loss is common in patients with OFCs and is associated with an increased risk of speech, language, and cognitive delays.22,23 Study data (patient characteristics, study design, country of origin, and results) were extracted by the authors independently, monitoring for agreement and resolving discrepancies by consensus.

Analysis
Results are reported descriptively, explaining differences in studies and potential sources of bias. We followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines for reviewing and presenting the data.24 Potential bias within and across studies was evaluated and discussed. We grouped studies according to age range to examine developmental trends in outcomes.

RESULTS
Study Characteristics
After the removal of 110 duplicates, we reviewed 2160 references and included 31 in the final review (Fig 1). Most articles were excluded because the outcome did not meet the inclusion criteria, the study population was limited to patients with a specific genetic diagnosis, or the study included ≤10 cases. The quality measures of the studies reviewed are summarized in Fig 2. Sixty-one percent of studies reported adequate demographic data (age, sex, and socioeconomic status [SES]), 65% of studies reported participation rate, and 65% of studies included a control group. More than one-half (58%) of studies included a clear description of how patients were determined to have syndromic or isolated clefts. Most articles included only patients with isolated clefts, but some included patients with syndromic clefts and analyzed them as a distinct subgroup. Thirty-five percent of the articles included adequate assessment of hearing status (eg, behavioral audiogram), 16% included limited hearing information (eg, frequency of otitis media), and 48% lacked information. Most studies (77%) were limited to a homogeneous sample (ie, patients with isolated OFCs). In all articles that included patients with syndromic OFCs, these patients were excluded from some analyses, although most studies did not have the sample size needed for examination of homogeneous clinical subgroups (eg, isolated versus syndromic OFCs).25 Authors of most studies used validated outcome measures and did not publish multiple articles on the same cohort.

Study characteristics are shown in Table 1, including author, title, study design, and number of participants. Overall, this review included 21 cohort and 10 cross-sectional studies. These studies included 10 143 patients with OFCs (2571 with CL, 4123 with CLP, 3357 with CP, and the remaining with syndromic clefts) and 2 017 361 controls.

Infancy and/or Toddler Age
Ten studies included infant and/or toddler participants: 9 cohorts and 1 case series. None used population-based samples, relying instead on recruitment through craniofacial clinics. Authors of 60% of studies reported adequate demographic data, authors of 30% of studies reported participation rate, and 60% of studies included a control group. Authors of only one-half of the studies reported clear methods for identifying syndromic patients, and authors of 50% of studies reported adequate hearing data. Most studies were
limited to nonsyndromic patients and used validated outcome measures. Compared with other age groups, there were fewer cases and controls represented in these studies (877 cases and 330 controls). Several of the studies were conducted in a single craniofacial center, used only 1 method for testing, and did not include a control group. In 1 study, all patients participated in early intervention services simply because they had OFCs compared with ∼50% of children in the control group.28

Numerous measurement outcomes were used in these studies, including both parent-reported (eg, MacArthur-Bates Communicative Development Inventories) and clinician-administered (eg, Bayley Scales of Infant Development) outcomes. Minimal differences were observed in parent-reported expressive language in a sample of 13-month-old children,26 but by 24 months of age, children with CL and CLP scored lower than controls, and group differences were correlated with degree of hearing loss.32 Children with bilateral CLP, but not CP or unilateral CLP, were reported to have delays in the use of 2- or 3-word phrases relative to controls.29 Expressive language in children with OFCs has also been shown to lag behind test norms, particularly for those with CP.31

Differences between cases and controls have also been observed in parent reports of receptive language and related constructs (eg, processing, attention, and memory).22,28 Measurable deficits appear by 12 to 36 months and were greatest for children with CP versus CL or CLP. Hearing is likely important for these outcomes but was not consistently reported. In at least 1 study, authors showed that although receptive language improved, hearing loss persisted in early childhood.31 Other parent-reported outcomes yielded similar findings, revealing motor delays at 5 months compared with normative values and worsening scores in multiple domains through toddler years.30

Among studies in which clinician-administered measures were used, several authors used the iterations of the Bayley Scales of Infant Development and showed deficits in motor and cognitive development relative to unaffected controls.22,27,33 For example, Speltz et al33 found delays in infants with clefts versus controls at ages 3, 12, and 24 months. Motor delays were more apparent at early ages and attenuated over time, although differences in cognition persisted. Differences were observed on both verbal and nonverbal cognitive items from the Bayley Scales of Infant Development, and children with CP performed worse than those with CLP or CL. Similar findings were observed in 2 other cohorts, again with children with CP performing worse than other cleft subgroups.32,34

### Early School-aged Children

Fourteen studies were focused on early school age development (ie, ∼5–10 years of age). Outcome measures included reading tests, IQ tests, or measurements related to grades or use of special education services. This group of studies included 5 cohorts and 9 cross-sectional studies. One-half of these studies reported adequate demographic data, 3 of 14 (21%) studies used population-based samples, and 79% of studies reported participation rates. Authors of 64% of studies presented clear methods of identifying syndromic patients, and most included a homogeneous group with a validated outcome measurement. Only 36% of studies included hearing data. Studies with this age group included the highest numbers of cases (4946 cases and 744,658 controls). There were several potential sources of bias among these studies. Participation rates were low for some studies,40 introducing the possibility of biases that are difficult to measure and fully account for statistically. For example, parents who are concerned about their child’s development may be more likely to participate as a means of receiving assessment. Alternatively, children who are doing well in school might be more interested and willing to take part in a study of these outcomes.36 A testing method relying on verbal responses can be subject to bias if the tester struggles to understand the
In general, and related outcomes, although some case-control differences in language Several studies in this group revealed lower scores than warranted. CP. Young et al46 studied expressive older (age 13), except for children with CLP when they were found that reading scores improved hearing loss was correlated with phonological processing) were found to be worse in children with OFCs –37,42 Authors of several studies found that children with OFCs were more likely to use special education services compared with unaffected peers.4,25,39 Although there was inconsistency in which type of OFC was most likely to use services, authors of the largest study found that children with CLP or CP were 3 times more likely than controls to use such services.25 Excluding patients receiving only speech therapy, children with OFCs were still more likely to receive services than controls (prevalence ratio = 1.6; 95% confidence interval: 1.0–2.4). Researchers also reported lower scores on standardized testing.

### TABLE 1

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Study Design</th>
<th>Patient Age</th>
<th>Cases, n</th>
<th>Controls, n</th>
</tr>
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<tbody>
<tr>
<td>Hardin-Jones and Chapman36</td>
<td>2014</td>
<td>Retrospective cohort</td>
<td>6–39 mo</td>
<td>37</td>
<td>22</td>
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<td>1996</td>
<td>Prospective cohort</td>
<td>12–24 mo</td>
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<td>2000</td>
<td>Retrospective cohort</td>
<td>4–36 mo</td>
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<td>12–36 mo</td>
<td>30</td>
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<tr>
<td>Nakajima et al29</td>
<td>2001</td>
<td>Retrospective cohort</td>
<td>18–24 mo</td>
<td>135</td>
<td>168</td>
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<td>Neirn and Savage20</td>
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<td>Retrospective cohort</td>
<td>5–36 mo</td>
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<td>Rueter et al31</td>
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<td>Retrospective cohort</td>
<td>20–76 mo</td>
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<tr>
<td>Snyder and Scherer32</td>
<td>2004</td>
<td>Prospective cohort</td>
<td>18–30 mo</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Speltz et al43</td>
<td>2000</td>
<td>Prospective cohort</td>
<td>3–24 mo</td>
<td>57</td>
<td>69</td>
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<td>Swanenburg de Veye et al34</td>
<td>2003</td>
<td>Cross-sectional</td>
<td>18 mo</td>
<td>148</td>
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<td>Chapman25</td>
<td>2011</td>
<td>Cross-sectional</td>
<td>5–6 y</td>
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<td>Collett et al4</td>
<td>2010</td>
<td>Prospective cohort</td>
<td>3–24 mo, 5–7 y</td>
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<td>Cross-sectional</td>
<td>5–7 y</td>
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<td>Eliason and Richman37</td>
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<td>Cross-sectional</td>
<td>4–6 y</td>
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<tr>
<td>Feragen et al38</td>
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<td>Cross-sectional</td>
<td>10 y</td>
<td>170</td>
<td>0</td>
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<tr>
<td>Fitzsimmons et al39</td>
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<td>Cross-sectional</td>
<td>10 y</td>
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<td>Knight et al40</td>
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<td>Retrospective cohort</td>
<td>5–12 y</td>
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<td>Laasonen et al41</td>
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<td>Lee et al42</td>
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<td>6–8 y</td>
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<tr>
<td>Richman et al42</td>
<td>1988</td>
<td>Cross-sectional</td>
<td>6–13 y</td>
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<tr>
<td>Richman et al44</td>
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<td>Cross-sectional</td>
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<td>Watkins et al46</td>
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<td>Retrospective cohort</td>
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<td>Yazdy et al25</td>
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<td>Retrospective cohort</td>
<td>3–10 y</td>
<td>777</td>
<td>737 928</td>
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<tr>
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<td>Retrospective cohort</td>
<td>3–6 y</td>
<td>43</td>
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<tr>
<td>Bell et al7</td>
<td>2017a</td>
<td>Retrospective cohort</td>
<td>6–15 y</td>
<td>402</td>
<td>1789</td>
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<tr>
<td>Bell et al47</td>
<td>2017b</td>
<td>Retrospective cohort</td>
<td>6–15 y</td>
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<td>2706</td>
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<td>Broder et al6</td>
<td>1998</td>
<td>Retrospective cohort</td>
<td>6–18 y</td>
<td>168</td>
<td>0</td>
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<tr>
<td>Clausen et al11</td>
<td>2017</td>
<td>Retrospective cohort</td>
<td>14–15 y</td>
<td>558</td>
<td>14 877</td>
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<tr>
<td>Conrad et al46</td>
<td>2014</td>
<td>Retrospective cohort</td>
<td>7–26 y</td>
<td>80</td>
<td>82</td>
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<tr>
<td>Persson et al43</td>
<td>2012</td>
<td>Retrospective cohort</td>
<td>18 y</td>
<td>1892</td>
<td>1 249 404</td>
</tr>
<tr>
<td>Wehby et al4</td>
<td>2014</td>
<td>Retrospective cohort</td>
<td>5–18 y</td>
<td>588</td>
<td>3735</td>
</tr>
</tbody>
</table>

The child’s speech,37 thereby resulting in lower scores than warranted.

Several studies in this group revealed case-control differences in language and related outcomes, although some revealed no differences.4 In general, reading and related skills (eg, phonological processing) were found to be worse in children with OFCs versus unaffected controls.35–37,42 Hearing loss was correlated with reading deficits.36 Richman et al43 found that reading scores improved for children with CLP when they were older (age 13), except for children with CP. Young et al15 studied expressive language in children in Singapore and found that children with clefts were more likely to have delays up to age 6, with no differences by cleft type, hearing status, or velopharyngeal adequacy. Authors of an additional study (with a lower quality score) found that patients with psychological adjustment problems were more likely to struggle with reading.38 Only one-half of these studies included a control group.

Authors of 3 studies in this age range (including 161 cases and 84 controls) measured IQ using the Wechsler Preschool and Primary Scale of Intelligence. Using data from a longitudinal study, Collett et al4 found that language measures at early school age were within the average range for children with OFCs and similar to controls. Among patients, Bayley Mental Developmental Index (MDI) scores and the quality of parent-child interactions in infancy were predictive of language outcomes at age 5. Authors of a small study reported no differences among IQ tests, but children with CP tended to have lower math scores, and children with CLP had higher verbal IQ scores.41 Authors of a third study found that IQ and reading scores of children aged 7 to 9 revealed a strong association between memory deficits and reading disability, reporting that 61% of children with memory deficits and clefts had reading disabilities compared with 30% of children without memory deficits.44

Authors of several studies found that children with OFCs were more likely to use special education services compared with unaffected peers.4,25,39 Although there was inconsistency in which type of OFC was most likely to use services, authors of the largest study found that children with CLP or CP were 3 times more likely than controls to use such services.25 Excluding patients receiving only speech therapy, children with OFCs were still more likely to receive services than controls (prevalence ratio = 1.6; 95% confidence interval: 1.0–2.4). Researchers also reported lower scores on standardized testing.
at 5 years of age across all domains for CLP or CP, with amplified effects for children from lower SES backgrounds. Authors of a survey with a 29% response rate found that children with OFCs aged 5 to 12 years were more likely to receive low grades and twice as likely to miss >5 days of school per year compared with peers, although they were not more likely to repeat a grade.\textsuperscript{40} Authors of a population-based study found lower performance in reading and math among children with OFCs for grades 3 to 8, with the strongest effect for children with CLP.\textsuperscript{15}

**Adolescence**

Authors of 7 articles, all retrospective cohorts, were focused on adolescence, measuring test scores or outcomes such as graduation rates and use of special education services. Five of 7 (71%) studies used population-based samples, and 86% of studies reported adequate demographic data and participation rates. Fifty-seven percent of studies reported methods for identifying syndromic patients, and only 1 of 7 (14%) of studies reported hearing data. This group of studies included 2 articles with potentially overlapping cohorts, although both were included in the review because they were focused on different outcomes.\textsuperscript{7,47} Because authors of some studies used existing data with large populations, the sample size was large, with 4320 cases and 1 272 373 controls represented. Some of the study designs may have introduced bias, such as 1 study in which authors did not adjust for confounding variables such as SES, maternal education, or race and/or ethnicity.\textsuperscript{6}

Of the researchers measuring standardized test scores, deficits in adolescence included math scores and were not limited to verbal scores as in younger ages.\textsuperscript{3,47} Children with OFCs were less likely to meet minimum standards in testing across all subject areas and ages tested. Deficits were largest among children with CP, but those with CLP and CL also showed worse performance than unaffected peers. A Danish study\textsuperscript{11} found that only children with CP had lower scores on the ninth-grade examination. Authors of 1 study who measured IQ in adolescents found that scores were within the average range but lower than the control group.\textsuperscript{46}

Authors of the remaining studies found deficits in other areas among children with OFCs, including grade retention and graduation rates. Among children in Western Australia, those with CLP had higher absenteeism in middle school but not high school, and absence rates were inversely associated with test scores.\textsuperscript{7} Authors of a study of 2 American centers found that children with OFCs and particularly boys with CP, who also had more grade retention and low test scores, were more likely to have learning disabilities.\textsuperscript{6} Authors of a Swedish study of graduation rates found that patients were less likely to graduate and received lower grades than controls.\textsuperscript{5} Youth with CP were most significantly affected, followed by children with CLP.

**DISCUSSION**

Nearly all studies reviewed revealed some degree of neurodevelopmental or academic deficit in children with OFCs compared with controls. This finding remained in large, methodologically rigorous studies, across several patient populations, and across a variety of outcome measures. Nonetheless, this does not mean that all children with OFCs are impacted, and future research should evaluate characteristics associated with risk for deficits. For example, finding a higher risk of deficits in clinical subgroups might help to identify targets for intervention such as amplification for children with hearing loss in addition to an oral cleft. Demographic subgroups found to be at particular risk (eg, children from lower SES backgrounds) might help to prioritize resources for screening and intervention. Descriptively, group differences were often small in magnitude but nonetheless important when considered from a public health perspective, given the prevalence of oral clefting. For example, Wehby et al\textsuperscript{3} found that children with OFCs scored 3 to 5 percentiles below unaffected classmates on standardized academic achievement measures. Even with this small shift in the distribution of their scores, children with clefts were more likely to score below a commonly used threshold for identifying learning problems and more likely than their peers to receive special education services. Therefore, children with OFCs are a population at risk for lower academic performance, and providers should be vigilant about advocating for appropriate support.

Several developmental trends were observed (Fig 3). During infancy and toddler years, receptive language and motor delays were evident at the youngest ages, followed by expressive language delays in children aged 12 to 24 months. Bayley MDI scores were lower for children with any cleft type, with differences persisting for mental but not psychomotor development. During the early school years, language and phonologic deficits were apparent and affected reading ability, particularly among children with CP with persistent hearing loss. Children with OFCs were more likely than unaffected peers to use special education services, including speech therapy as well as other educational interventions. This suggests that existing systems of care identify children with OFCs for intervention, although the adequacy of interventions are unclear, and children show persistent academic deficits through adolescence. School absences were more common during middle school but not high school. This is consistent with the typical course of craniofacial care, with
a higher burden of care during elementary and middle school versus high school. Children with OFCs also had lower graduation rates, suggesting a long-term impact of academic differences.

Children with CP generally had the poorest outcomes compared with other cleft types, but this was inconsistent, and subgroup comparisons were often limited by small sample size. Additional research may elucidate risks associated with specific cleft types. Distinct embryologic processes lead to the formation of the lip and the palate, and differences in outcomes may be related to these processes. The associated risk of additional malformations, which may contribute to neurodevelopmental deficits, is greater for children with CP than for CLP. If structural brain differences are associated with OFCs, as has been suggested, these may be specific to cleft type and impact academic outcomes.

Limitations in the existing literature may have impacted our conclusions. First, the quality of the studies was variable. Low numbers of children with OFCs at most centers led to studies with small samples and precluded meaningful subgroup analyses. There were only 8 population-based studies (mostly in adolescents), with authors of others recruiting patients from craniofacial centers. Clinic-based sampling may introduce bias. Patients may differ from the community on the basis of demographic factors (e.g., SES) or may over-represent more severely affected children. Given these potential biases, a methodologic shortcoming was that authors of several studies (n = 11) did not report participation rate or provide a comparison of participants and nonparticipants. Authors of numerous studies relied on parent surveys to assess children’s usage of special education services or grade retention, often with low participation rates, which increases the risk of bias. Additionally, authors of many studies did not include an unaffected control group, instead relying on comparison with test norms. Although clinically useful, test norms do not necessarily reflect the demographic characteristics of patient samples. Despite the variable quality, however, there were several high-quality studies in each age group that revealed academic deficits in various domains for children with OFCs.

The heterogeneity among these studies not only prevented a meta-analysis, but also contributed to limitations in several areas. For example, 7 studies included patients with possible syndromes. These patients are known to be more likely than children with isolated clefts to have neurodevelopmental delays and
would ideally be evaluated as a distinct subgroup. However, most studies lacked the sample size needed for stratified analyses. Only 18 studies had a rigorous method for categorizing a patient as having syndromic clefts. Without clearly distinguishing these patients, the results could overestimate the differences among groups. Researchers inconsistently described confounding factors (eg, whether a child attended preschool, had an older sibling, or received support through early intervention) that may impact development. Other potential confounding factors that were seldom addressed in the literature included the number of surgeries the child received, whether the child had surgery at the recommended age, and whether the child received care through an accredited multidisciplinary craniofacial team. Hearing loss was not consistently reported, with only 11 studies (mostly of younger children) including hearing as a potential mediating variable. We believe that results from audiograms or some other standardized hearing assessment should be included in future studies.

Although this is the most comprehensive systematic review completed to date, we limited our focus to articles in English and studies completed in middle- or upper-income countries. This may have excluded studies that would contribute to our understanding of development in children with clefts across sociodemographic and cultural settings. Similarly, we did not include studies with a primary emphasis on speech outcomes, although this clearly relates to neurodevelopmental outcomes of interest.

This review highlights several modifiable targets for interventions that could improve neurodevelopmental and academic outcomes for children with OFCs. Among the most consistent findings in this literature is that children with OFCs struggle academically, particularly in reading and language-dependent subjects. Existing systems of care appear to identify these children as needing additional support (ie, higher rates of special education service), although the nature and adequacy of this support are unclear. Additional research testing strategies to promote early literacy are needed. Hearing is another promising target for intervention. For example, closer monitoring of hearing as a part of craniofacial care and more aggressive use of early amplification may promote early language outcomes with downstream benefits for school achievement. Other potential targets of intervention are less clearly defined, such as differences in feeding and bonding patterns in infants with OFCs and the psychosocial impact of OFCs on a child’s school performance. Although there has been concern about the potential neurotoxic effects of anesthesia exposure in early childhood, the 1 study in which this was investigated in a cleft sample did not reveal significant associations. In addition, in noncleft samples, authors of recent studies have been reassuring and have shown negligible effects related to brief anesthesia exposure.52

Similarly, differences in school attendance among children with clefts do not appear to account for observed differences in school achievement. Clearly, providers will still want to be mindful of the burdens imposed by the number of surgeries and frequency of clinic visits, but overall these do not appear to be significant contributors to neurodevelopmental and/or academic deficits.

CONCLUSIONS

On average, children with OFCs are at risk for poorer developmental and academic outcomes when compared with unaffected peers. Although these findings do not imply that all children with OFCs will exhibit poor neurodevelopmental outcomes, providers should monitor development and school performance closely and advocate for support when needed. It is possible that some conclusions are drawn from studies that included patients with syndromic forms of clefting, inadequately treated hearing loss, testing methods that did not consider the impact of a cleft-related speech disorder, or other factors that would negatively impact observed outcomes. Future research should include a rigorous review of participants to identify syndromic cases and assessment of hearing status while attempting to minimize bias and include a more representative sample of participants. The development of interventions to improve outcomes in several identified domains, such as preliteracy skills and hearing loss, may help narrow the academic gap for this vulnerable population.

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ABBREVIATIONS

CL: cleft lip
CLP: cleft lip and palate
CP: cleft palate
MDI: Mental Developmental Index
OFC: orofacial cleft
PDI: Psychomotor Developmental Index
SES: socioeconomic status
REFERENCES


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